Treatment Response, Relapse, and Survival of Hospitalized Adult Primary Warm Autoimmune Hemolytic Anemia: a Multicenter Retrospective Cohort Study

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Key Takeaway

- This study enhances the understanding of clinical characteristics of patients with wAIHA, and generates evidence of treatment, response, relapse and survival in practice.
- The results highlights high response rate with limited control time and poor survival in Chinese wAIHA patients, emphasizing the need for improved medical interventions and support for affected populations in China.

Conclusions

- In Chinese patients with primary wAIHA, while favorable treatment responses were observed after therapy, there was a notably high rate of relapse accompanied by limited periods of control and poor survival, particularly following hospitalization.
- This transient relief along with the poor survival outcomes presents a substantial healthcare burden and highlights an urgent need for innovative therapeutic options that can offer more stable and long-term effective treatment for patients with primary wAIHA in China.

Introduction

- Primary warm autoimmune hemolytic anemia is a rare autoimmune disease leading to accelerated red-cell destruction and anemia.
- Due to its rarity, the treatment choice is based on physician's experience and expert guidelines, and evidence on the treatment response, subsequent relapse and prognosis is not well-understood, especially in China, which are important to inform clinical management of the disease.

Aim

- This study aims to inform evidence-based management for wAIHA by describing the treatment response of adult patients hospitalized with primary wAIHA and assessing relapse and survival following treatment.

Methods

- **Study design**: longitudinal observational cohort study.
- **Data source**: utilized electronic medical records (EMR) from three hospitals in Shanghai. Data on demographic, diagnosis history, hemolysis characteristics, treatment and response were collected from the EMR. Relapse, survival and missing information of response were obtained by physicians through post discharge follow-up phone calls until November 15, 2024.
- **Study population**: adult patients with at least one confirmed diagnosis of wAIHA while hospitalized between 01 January 2014 and 31 March 2024 in one of three hospitals.

- **Outcome**: treatment response, relapse and survival assessed.
  - Definition:
    - Complete response (CR): normalization of hemoglobin.
    - Partial response (PR): an increase in hemoglobin > 20 g/L but not normal and absence of transfusion for the previous 7 days.
    - Relapse: a decrease in hemoglobin > 20 g/L after reaching PR, or a reappearance of wAIHA after reaching CR.
- A logistic regression model was conducted to investigate the factors associated with relapse. The optimal cutoff point for continuous variables were determined and applied in the models.
- The age-standardized mortality rate was calculated based on the age composition of the 2020 Chinese National Population Census using direct standardization.

Results

- A total of 104 primary wAIHA patients were included (Figure 1)
- Patients were at elder age, with multiple comorbidities and in poor health conditions. Most patients presented moderate and severe anemia, with elevated Ret, TBIL and LDH, indicating increased red blood cell destruction (Figure 2).
- Corticosteroids (CS) is the mainstay for 1L treatment. The overall response was high while the relapse rate was also high with limited control time (Figure 2).

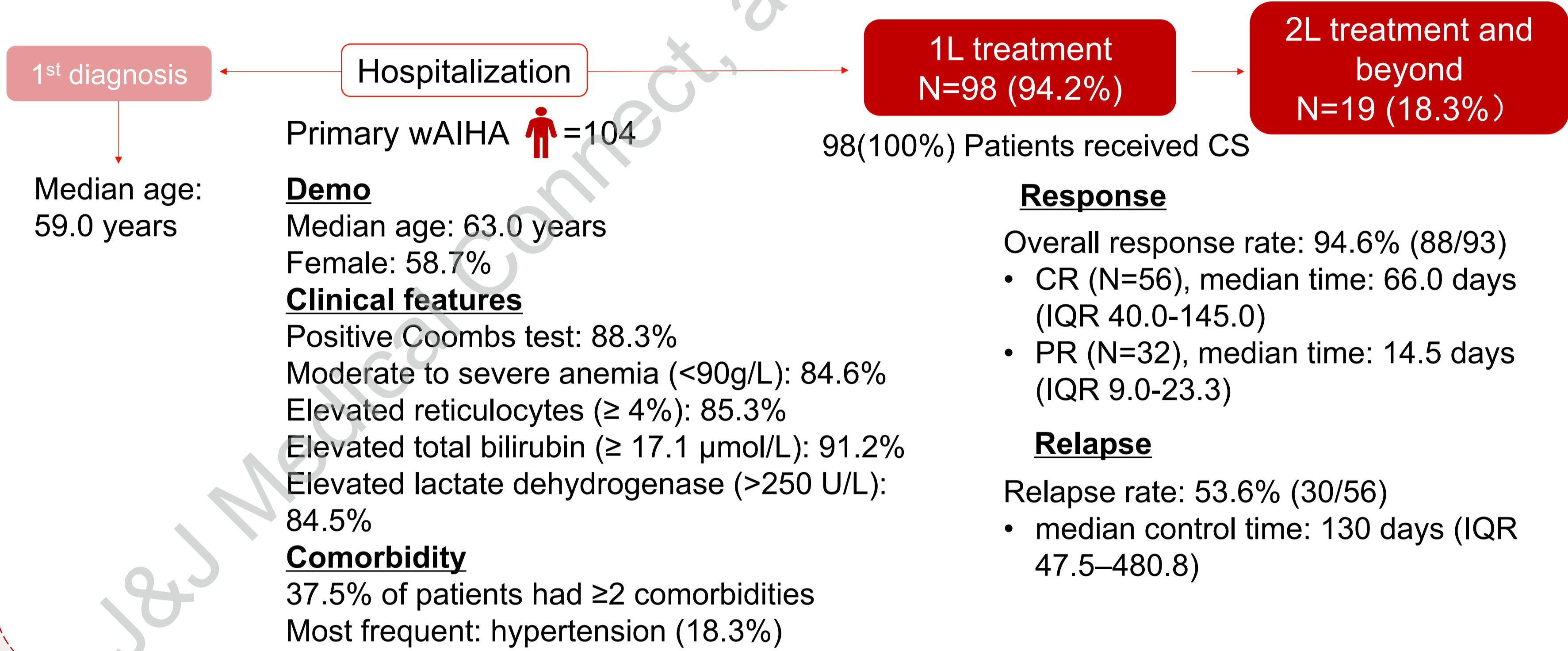Figure 2. Demographics, clinical features, treatment response and relapse

1st diagnosis → Hospitalization → 1L treatment N=98 (94.2%) → 2L treatment and beyond N=19 (18.3%)

Primary wAIHA 👤 =104
98(100%) Patients received CS

Median age: 59.0 years

Demo
Median age: 63.0 years
Female: 58.7%
Clinical features
Positive Coombs test: 88.3%
Moderate to severe anemia (<90g/L): 84.6%
Elevated reticulocytes (≥ 4%): 85.3%
Elevated total bilirubin (≥ 17.1 μmol/L): 91.2%
Elevated lactate dehydrogenase (>250 U/L): 84.5%
Comorbidity
37.5% of patients had ≥2 comorbidities
Most frequent: hypertension (18.3%)

Response
Overall response rate: 94.6% (88/93)
- CR (N=56), median time: 66.0 days (IQR 40.0-145.0)
- PR (N=32), median time: 14.5 days (IQR 9.0-23.3)

Relapse
Relapse rate: 53.6% (30/56)
- median control time: 130 days (IQR 47.5–480.8)

Figure 1. Patient selection flowchart

Hemolytic anemia inpatients in three hospitals from January 2014 to March 2024
N= 366

Excluded:
- 3 patients <18y
- 156 patients not meet the diagnostic criteria of AIHA

Patients with AIHA
N= 207 (56.6%)

Excluded:
- 5 patients with cold AIHA

Patients with wAIHA
N=202 (97.6%)

Excluded:
- 98 patients with secondary wAIHA
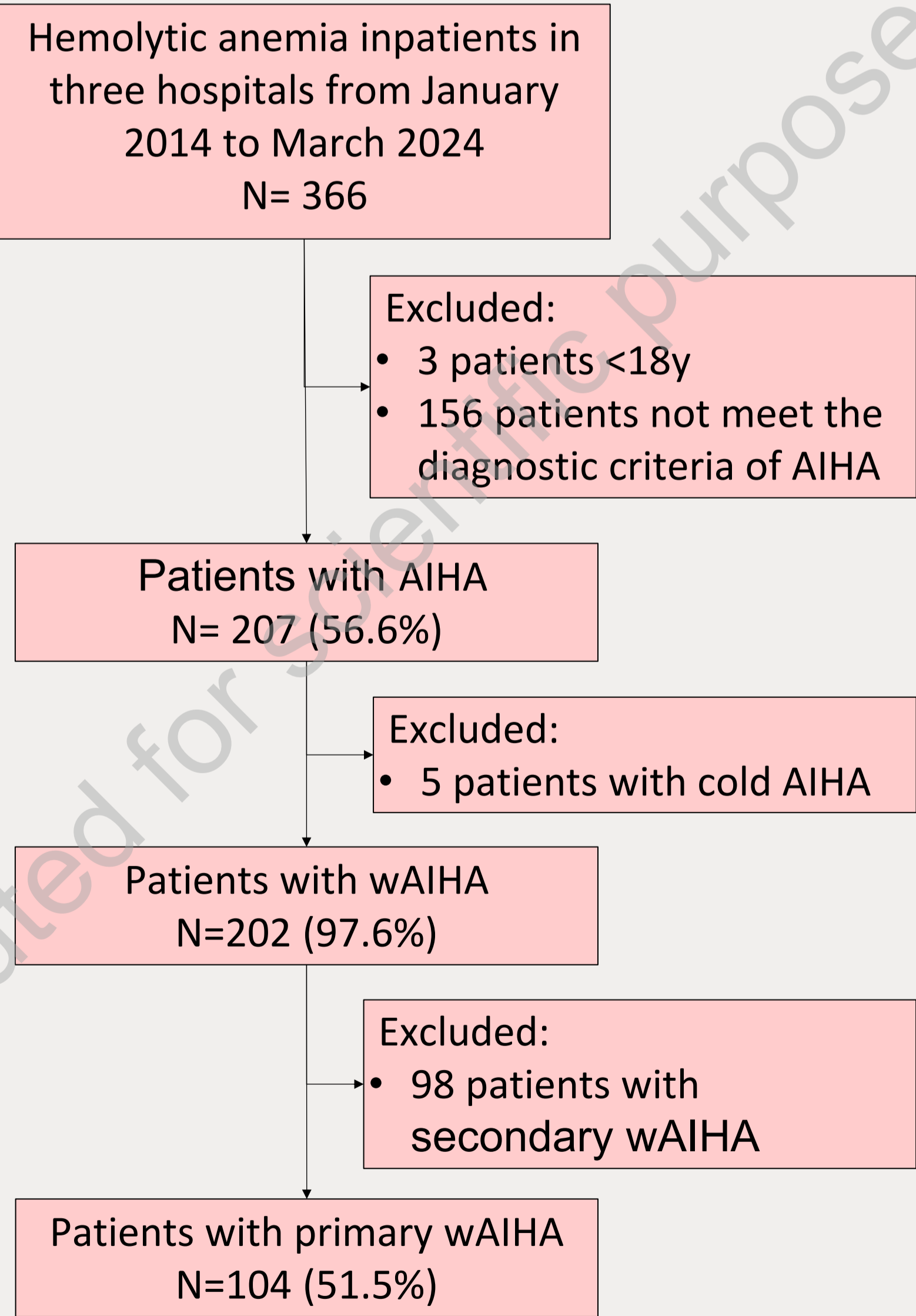
Patients with primary wAIHA
N=104 (51.5%)

Table 1. Logistic regression analysis for the risk factors of relapse in patients with primary wAIHA

Variables	Univariate logistic regression		Multivariate logistic regression	
	OR (95%CI)	P-value	OR (95%CI)	P-value
Age (≥ 60)	0.892 (0.310–2.566)	0.832		
Male	1.364 (0.474–3.925)	0.565		
Coombs test	1.548 (0.368–6.500)	0.551		
Hb levels (< 50g/L)	1.917 (0.428–8.584)	0.395		
Reticulocyte percentage (≥ 14%)	4.286 (1.264–14.531)	0.019	**4.540 (1.273–16.197)**	**0.020**
Total bilirubin (≥ 51.3μmol/L)	0.846 (0.289–2.481)	0.761		
Indirect bilirubin (≥ 36μmol/L)	0.636 (0.217–1.863)	0.409		
LDH (≥ 375 U/L)	2.164 (0.713–6.570)	0.173		
WBC (≥ 4 x10⁹/L)	0.986 (0.284–3.421)	0.982		
PLT (≥ 200 x10⁹/L)	0.875 (0.306–2.504)	0.803		
Number of complication (≥1)	2.722 (0.909–8.157)	0.074	3.037 (0.920–10.024)	0.068
Complication: EVANS syndrome	0.846 (0.189–3.784)	0.827		
Complication: Infection	2.222 (0.691–7.151)	0.181		

Note: OR, odds ratio; CI, confidence interval; Hb, hemoglobin; LDH, lactate dehydrogenase; WBC, white blood cell count; PLT: platelet count

- 31.7% (33/104) of the patients died during follow-up period, and infection was the most common reason (20.2%，21/104), followed by hemolytic anemia (2.9%，3/104).
- The median OS following hospitalization was not reached, when considering the whole disease course from 1st diagnosis, the estimated median OS was 278.3 month (Figure 3). At 1-, 3- and 5-year post hospitalization, the accumulative death rates were 15.7%, 23.7% and 34.8%, and were 8.9%, 14.3% and 20.3%, respectively, from the 1st diagnosis.
- The age-standardized rate of death was higher than the rate in general population (23.1% vs. 0.7%)
- The reticulocyte percentage ≥ 14% at hospitalization (aOR=4.54, p=0.020) was an independent risk indicator for relapse (Table 1)

Figure 3. KM plot of survival of patients with wAIHA

Median OS (95%CI): NA (66.2, NA)

Median OS (95%CI): 278.3 (117.3, NA)
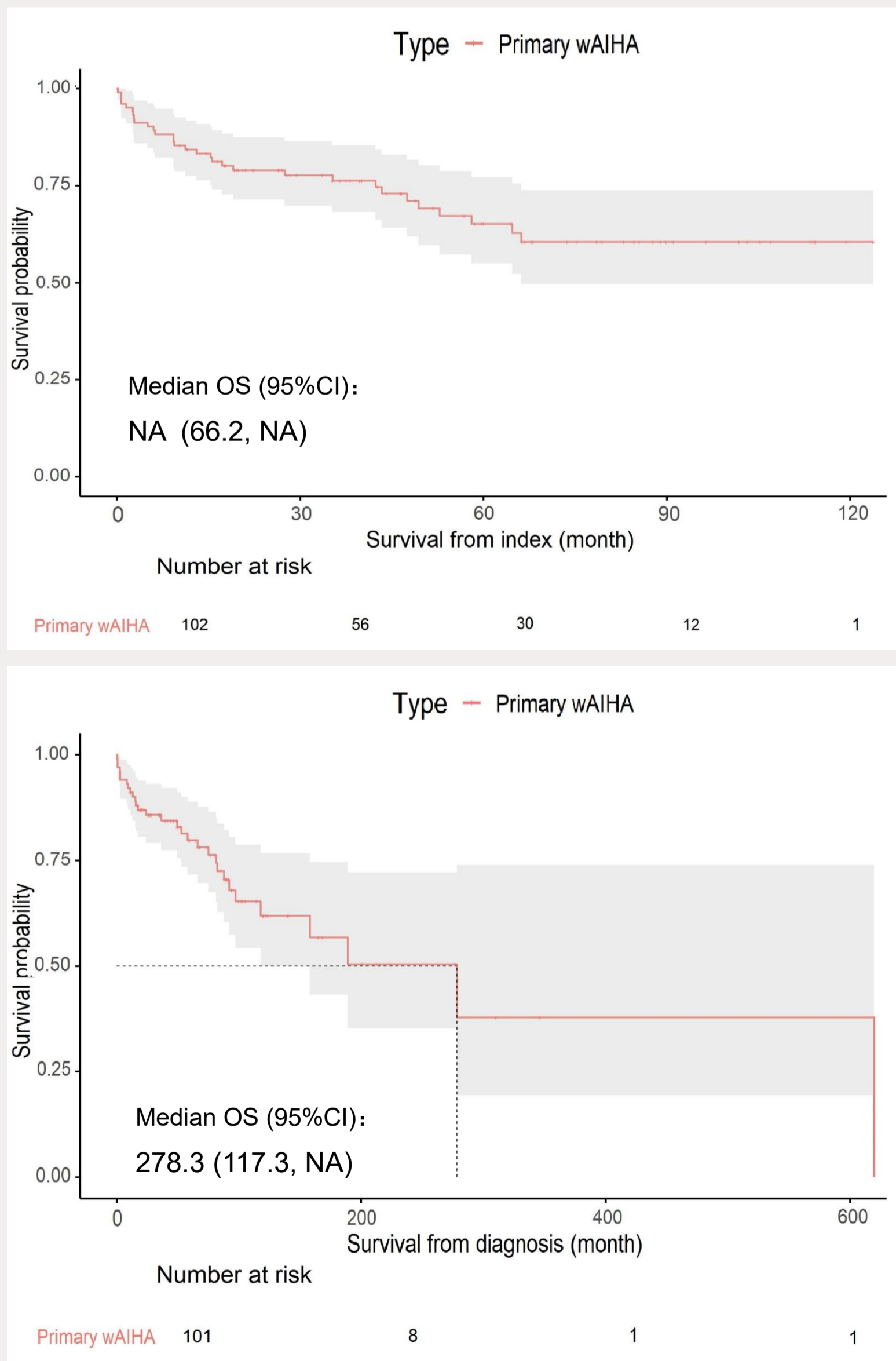
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